Procter&Gamble

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November 4, 1999

Documents Management Branch
Food and Drug Administration
HFA-305
5630 Fishers Lane.
Rm. 1061
Rockville, MD 20852

Re: Docket Number 97D-0433

Dear Sir or Madam:

Procter & Gamble Pharmaceuticals has reviewed the Draft Guidance for Industry, Average, Population, and Individual Approaches to Establishing Bioequivalence. We have the following comments.

1. IV. Bioequivalence Criteria -- These approaches must assure internal consistency in hierarchical inferences. Statistics should be developed so that individual bioequivalence implies population and population implies average bioequivalence. In addition, the assessment criteria should include a maximum allowable mean difference.

2. VII.A. Studies in Multiple Groups -- Performing a study at two or more sites or at the same site but at different times is very unlikely to introduce a bias in a crossover study that would result in a conclusion of equivalence when the products were, in fact, not equivalent. Consequently, any decisions regarding multiple groups should be at the discretion of the sponsor and FDA should not routinely expect a statistical model that reflects the multigroup nature of the study.

3. VII.C.1. Product Failure – The appearance of product failure can be caused by a variety of phenomena. These can be related to actual product performance or they could relate to variation in gastric emptying or GI transit. Additional guidance regarding how to deal with products that occasionally appear to not perform would be useful.

If there are any questions or if I can be of further assistance, feel free to call on me. My phone number is 513-622-3914 and my email address is welles.hl@pg.com.

Sincerely,

Harry L Welles

Harry L. Welles, Ph.D.
Principal Scientist
Regulatory Affairs

97D-0433

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